

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on 3/18/02

Shaylor B. Outhn Date of Signature 3/18/02 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Malouf et al.

Examiner: Not Assigned

Application No.: 10/029,413

Group Art Unit: Not Assigned

Filed: December 20, 2001

Docket No.: 421/29/2

Confirmation No.: 3695

or: PURIFIED AND ISOLATED PLATELET CALCIUM CHANNEL NUCLEIC ACIDS AND POLYPEPTIDES AND THERAPEUTIC AND SCREENING METHODS

USING SAME

U.S. Patent and Trademark Office BOX SEQUENCE P.O. Box 2327 Arlington, Virginia 22202 **RECEIVED**

JUL 3 2002

TECH CENTER 1600/2900

TRANSMITTAL OF FORMAL DRAWINGS

Dear Sir:

Please find enclosed a new set of formal drawings (17 sheets) for filing in the above-identified U.S. Patent Application.

Although a check is being submitted, the Commissioner is hereby authorized to charge any deficiencies of payment associated with the filing of this correspondence to Deposit Account No. 50-0426.

Respectfully submitted,

JENKINS & WILSON, P.A.

Date: 03/18/2002

Rv.

Arles A. Taylor, Jr. Registration No. 39,395

Suite 1400 University Tower 3100 Tower Boulevard Durham, North Carolina 27707

Telephone: (919) 493-8000 Facsimile: (919) 419-0383

Customer No. Bar Code Label:

421/29/2

AAT/JAL/sed

25297

PATENT TRADEMARK OFFICE

Title: Purified and Isolated Platelet and Calciu'r Acids and Polypeptides and Therapeutic a pplicant(s): Malouf et al.
Serial No.: 10/029,413 Title: annel Nucleic

FIG. 1A

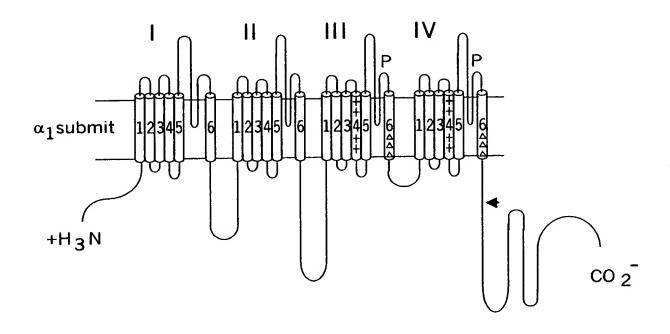
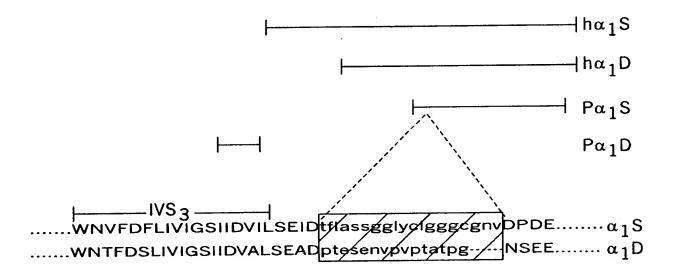


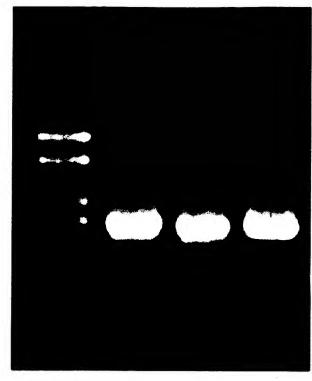
FIG. 1B



Fitle: Purified and Isolated Platelet and Calcium Canel Nucleic Acids and Polypeptides and Therapeutic and Sening

Serial No.: 10/029,413

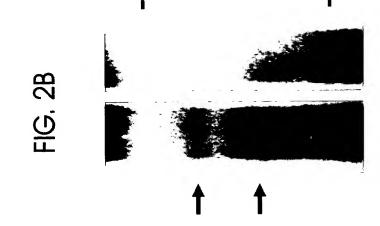
FIG. 1C



1 2 3

FIG. 1D

App t(s): Malouf et al. Serial No.: 10/029,413



Έ

国

8

4

Acids and Poly Aparth (s): Malouf et al. Serial No.: 10/029,413

>ref|xx 001910.1| Homo sapiens calcium channel, voltage-dependent, L type, alpha 1S subunit (CACNAIS), mRNA, Length = 6615

Score = 79.8 bits (40), Expect = le-l2 Identities = 46/48 (95%) Strand = Plus / Plus

3985 ctgattgtcattggcagcatcattgatgtcatcctcagtgagatcgac ctgattgtcatcggcagcatcattgacgtcatcctcagtgagatcgac Sbjct: 3938 Query: 1

Score = 622 bits (314), Expect = e-176 Identities = 462/510 (90%), Gaps = 1/510 (0%) Strand = Plus / Plus

4102 gacccagatgagagtgcccgcatctccagcgccttcttccgcctgttccgtgtcatgagg gaccccgacgagagtgcccgcatctccagcgccttcttccgcctgttccgggtcatgagg Sbjct: 4043 Query: 49

4162 168 Sbjet: 4103 etgatcaagetgetgageegggeagaaggagtgegaaeeeteetgtggaegtteateaag ttgatcaagctgctgagccgcgcgagggcgtgcgcacgctgctccggaccttcatcaag Query: 109

tecttecaggecetgecetacgtggetetgeteategteatgetettetteatetatget Query: 169

4222 tecttecaggeectacectacgtggetetgeteategteatgetettetteatetacget Sbjct: 4163

FIG. 3A

Acids and Polyp Eant(s): Malouf et al. Serial No.: 10/029,413

FIG. 3B

4342 4282 aacaacaacttccagaccttcccacaagctgtgctactgctcttcaggtgtgcaacaggt gtcatcggcatgcagatgtttgggaagatcgccttggtggatgggacccaaataaaccgg aacaacaatttccagacettccctcaggetgtgctgctgctcttcaggtgcgccacgggt gtcatcggcatgcagatgtttgggaagatcgccatggtggacggaaccagg Sbjct: 4283 Sbjct: 4223 Query: 289 Query: 229

gaggeetggeaggagateetaetggeetgeagetatgggaagetgtgtgaeeeagagteg 4402 gaggcgtggcaggatcctgctggcctgcaggtacgggcagctgtgcgaccccgagtca Sbjct: 4343 Query: 349

4462 gactatgccccaggggaggagtacacatgtggcaccaactttgcatactactactcatc gactacctccctggggaggagtatacctgcggcaccgacttcgcctactacttcatc Sbjct: 4403 Query: 409

4522 528 agettetacatgetetgtgeetteetggteateaaeetettgtggetgteateatggae agettetacatgetetgtgeetteetgateateaaeetettgtggetgtgateatggae Sbjct: 4463 Query: 469

Query: 529 aattttgactacctcaccc-ggactggtcc 557

Sbjet: 4523 aattttgactaceteaceegggactggtee 4552

Title: Serial No.: 10/029,413

FIG. 3C

Homo sapiens calcium channel, voltage-dependent, L type, (CACNAIS), mRNA, Length = 6160 alpha 1S, subunit >ref|NM 000069.1|

Score = 79.8 bits (40), Expect = le-12 Identities = 46/48 (95%) / Plus Strand = Plus

3834 Sbjet: 3787 etgattgteattggeageateattgatgteatecteagtgagategae Query: 1

Identities = 462/510 (90%), Gaps = 1/510 (0%) Strand = Plus / Plus Score = 622 bits (314), Expect = e-176

3951 108 gacccagatgagagtgcccgcatctccagcgccttcttccgcctgttccgtgtcatgagg gaccccgacgagagtgcccgcatctccagcgccttcttccgcctg Sbjct: 3892 Query: 49

4011 ctgatcaagetgetgageegggeagaaggagtgegaaceeteetgtgaegtteateaag trgatcaagetgetgageegegeegaggegtgegeaegetgeteeggaeetteateaag Sbjct: 3952 Query: 109

teetteeaggeectacectaegtggetetgeteategteatgetettetteatetaeget 4071 tocttecaggecetgecetacgtggetetgeteategteatgeteteteteatetatget Sbjct: 4012 Query: 169

Purified and Isolated Platelet and Calcium Channel Title: ids and Polypeptides and Therapeutic and Screening Malouf et al.

Serial No.: 10/029,413

FIG. 3D

4311 4191 4131 gaggegtggcaggatectgetggeetgcaggtacgggcagetgtgcgaceegagtca gaggcctggcaggagatcctactggcctgcagctatgggaagctgtgtgacccagagtcg gactatgccccaggggaggagtacacatgtggcaccaactttgcatactacttcatc aacaacaacttccagaccttcccacaagctgtgctactgctcttcaggtgtgcaacaggt gactacctccctggggaggagtatacctgcggcaccgacttcgcctactactcatc gtcatcggcatgcagatgtttgggaagatcgccttggtggatgggacccaaataaaccgg aacaacaatttccagaccttccctcaggctgtgctgctgctcttcaggtgcgccacgggt gtcatcggcatgcagatgtttgggaagatcgccatggtggacggaacccagataaaccgg Sbjct: 4252 Sbjct: 4192 Sbjct: 4132 Sbjct: 4072 Query: 409 Query: 349 Query: 229 Query: 289

4371 Sbjet: 4312 agettetacatgetetgtgeetteetggteatcaacetetttgtggetgteateatggae agettetacatgetetgtgccttectgateateaacetettgtgggctgtgateatggae Query: 469

aattttgactacctcaccc-ggactggtcc Query: 529

4401 aattttgactacctcacccgggactggtcc Sbjct: 4372

Serial No.: 10/029,413

FIG. 3E

>gb|L33798.1|HUMCACNLA Human dihydropyridine-sensitive L-type calcium channel alpha-1 subunit (CACNL1A3) mRNA, complete cds, Length = 6160

Score = 79.8 bits (40), Expect = le-l2 Identities = 46/48 (95%) Strand - Plus / Plus

3834 Sbjet: 3787 etgattgteattggeageateattgatgteatecteagtgagategae ctgattgtcatcggcagcatcattgacgtcatcctcagtgagatcgac Query: 1

Identities = 462/510 (90%), Gaps = 1/510 (0%) Score = 622 bits (314), Expect = e-176 Strand = Plus / Plus

3951 gacccgacgagagtgcccgcatctccagcgctttccgcctgttccgggtcatgagg 108 Sbjet: 3892 gacccagatgagagtgcccgcatetecagcgccttcttccgcctgttccgtgtcatgagg Query: 49

Sbjct: 3952 ctgatcaagctgctgagccgggcagaaggagtgcgaacctcctgtggacgttcatcaag 4011 trgatcaagetgetgageegeegeegaggegtgegeaegetgeteeggaeetteateaag 168 Query: 109

Title: Purified and Isolated Platelet and Calcium Characteristic Acids and Polypeptides and Therapeutic and Screening Appoint(s): Malouf et al.

Serial No.: 10/029,413

| 469 agettetacatgetetgtgeetteetgateateaaeetetttgtggetgtgateatggae 528 | Query: 469 |
|---|---|
| | Sbjct: 4312 |
| 109 gactacctccctggggaggagtatacctgcggcaccgacttcgcctactacttcatc 468 | Query: 409 |
| | Sbjct: 4252 |
| 149 gaggegtggeaggagatectgetggeetgeaggtaegggeagetgtgegaeeeegagtea 408 | Query: 349 |
| | Sbjct: 4192 |
| 89 aacaacaatttccagaccttccctcaggctgtgctgctgctcttcaggtgcgccacgggt 348 | Query: 289 |
| | Sbjct: 4132 |
| 29 gtcatcggcatgcagatgtttgggaagatcgccatggtggacggaacccagataaaccgg 288 | Query: 229 g' Sbjct: 4072 g |
| 9 teetteeaggeeetgeestacgtggetetgeteategteatgeteeteeteeteategee 12. | Query: 169 Sbjct: 4012 |

557

aattttgactacctcaccc-ggactggtcc

Query: 529

FIG. 4A

>ref|xxx 001910.1| Homo sapiens calcium channel, voltage-dependent, L type, alpha 1S subunit (CACNA1S), mRNA, Length = 6615

Score = 107 bits (54), Expect = 5e-21 Identities = 63/66 (95\$)Strand = Plus / Plus

3979 tggaatgtgtttgacttcctgattgtcattggcagcatcattgatgtcatcctcagtgag tggaatgtgttcgacttcctgattgtcatcggcagcatcattgacgtcatcctcagtgag Sbjct: 3920 Query: 1

Sbjct: 3980 accgac 3985 atcgac Query: 61

Score = 507 bits (256), Expect = e-141 Identities = 388/432 (89%) Strand = Plus / Plus

4102 gacccagatgagagtgcccgcatctccagcgccttcttccgcctgttccgtgtcatgagg gaccccgacgagagtgcccgcatctccagcgccttc Sbjct: 4043 Query: 67

ctgatcaagctgctgagccgggcagaaggagtgcgaaccctcctgtggacgttcatcaag 4162 ttgatcaagetgetgageegegeegaggegtgegeaegetgetetggaeetteateaag Sbjct: 4103 Query: 127

s): Malouf et al. Applid Serial No.: 10/029,413

FIG. 4B

4462 4342 4402 4282 4222 gactatgccccaggggaggagtacacatgtggcaccaactttgcatactacttcatc gaggcctggcaggagatcctactggcctgcagctatgggaagctgtgtgacccagagtcg gaggcgtggcaggatcctgctggctgcaggtacgggcagctgtgcgaccccgagtca gactacctccctggggaggagtatacctgcggcaccgacttcgcctactactcatc teettecaggecetacectacgtggetetgeteategteatgetettetteatetacget gtcatcggcatgcagatgtttgggaagatcgccatggtggacggaacccagataaaccgg gtcatcggcatgcagatgtttgggaagatcgccttggtggatgggacccaaataaaccgg aacaacaacttccagaccttcccacaagctgtgctactgctcttcaggtgtgcaacaggt tecttecaggecetgeectacgtggetetgeteategteatgetettetteatetatget aacaacaatttccagacettccetcaggetgtgetgetgetettcaggtgcgccacggg Sbjct: 4403 Sbjct: 4343 Sbjct: 4283 Sbjct: 4223 Sbjct: 4163 Query: 427 Query: 247 Query: 367 Query: 307 Query: 187

Query: 487

Sbjct: 4463 agettetacatg

FIG. 5A

>ref(xxx 003238.1] Homo sapiens calcium channel, voltage-dependent, L type, alpha 1D subunit (CACNAlD), mRNA, Length = 7362

Score = 89.7 bits (45), Expect = le-15 Identities = 45/45 (100%) Strand = Plus / Plus

ctcatcgtaatcggcagcattatagacgtggccctcagcgaagca 4215 ctcatcgtaatcggcagcattatagacgtggccctcagcgaagca Sbjct: 4171 Query: 1

Identities = 496/500 (99%), Gaps = 2/500 (0%) Strand = Plus / Plus 946 bits (477), Expect = 0.0 Score =

aactctgaagagagcaatagaatctccatcaccttttccgtctttccgagtgatgcga 4323 108 aactetgaagaggaatagaateteeateaeetttteegtettteegagtgatgega Sbjct: 4264 Query: 49

ttggtgaagetteteageagggggaaggeateeggaeattgetgtggaettttattattaag 4383 ttggtgaagetteteageagggggaaggeateeggaeattgetgtggaettttattaag: 168 Sbjct: 4324 Query: 109

teettteaggegeteeegtatgtggeeeteeteatageeatgetgttetteatetatgeg 4443 teettteaggegeteegtatgtggeeeteeteatageeatgetgttetteatetatgeg Query: 169

Sbjct: 4384

Purified and Isolated Platelet and Calcium Chan Acids and Polypeptides and Therapeutic and Scre t(s): Malou 198 Title: Nucleic

Serial No.: 10/029,413

FIG. 5B

| 4503 | 348 4563 | 408 |
|--|---|--|
| gtcattggcatgcagatgtttgggaaagttgccatgagagataacaaccagatcaatagg | aacaataacttccagacgtttccccaggcggtgctgctcttcaggtgtgcaacaggt | gaggeetggeaggagateatgetggeetgteteceagggaagetetgtgaeeetgagtea |
| 4444 | 289 4504 | 349 4564 |
| Query: 229 Sbjct: 444 | Qu e ry: Sbjet: | Query: Sbjct: |

Sbjet: 4624 gattacaaceceggggaggagtatacatgtgggagcaactttgecattgtetatttcate 4683 gattacaacctcggggaggagtatacatgtgggagcaactttgccattgtctatttcatc Query: 409

Sbjet: 4684 agettetacatgetetgtgcatttetgateatetatetgttt-gtggetgtcatcatgga 4742 527 agnttttacatgetetgtgcatttetga-cateaatetgtttggtggetgteatgga Query: 469

taatttcgactatctgaccc Query: 528

4762 taatttcgactatctgaccc Sbjct: 4743

ant(s): Malouf et al. Serial No.: 10/029,413

FIG. 5C

>ref|NM 000720.1| Homo sapiens calcium channel, voltage-dependent, L type, alpha 1D subunit (CACNAlD), mRNA, Length = 7193

Score = 87.7 bits (44), Expect = 5e-15 Identities = 44/44 (100%) Strand = Plus / Plus

ctcatcgtaatcggcagcattatagacgtggccctcagcgaagc 4044 ctcatcgtaatcggcagcattatagacgtggccctcagcgaagc Sbjct: 4001 Query: 1

Identities = 496/500 (99%), Gaps = 2/500 (0%)
Strand = Plus / Plus 946 bits (477), Expect = 0.0 Score =

aactetgaagagageaatagaateteeateacetttteegtettteegagtgatgega 4153 aactotgaagagagcaatagaatotocatoacottttoogtottttoogagtgatgoga 108 Query: 49

Sbjct: 4094

ttggtgaagetteteageaggggaaggeateeggaeattgetgtggaettttattaag 4213 168 ttggtgaagetteteageaggggaaggeateeggacattgetgtggaettttattaag Sbjct: 4154 Query: 109

228 teettteaggegeteeegtatgtggeeeteeteatageeatgetgttetteatetatgeg Query: 169 4273 teettteaggegeteeegtatgtggeeeteeteatageeatgetgttetteatetatgeg Sbjct: 4214 Title: Serial No.: 10/029,413

FIG. 50

4513 4572 4393 4453 4333 288 gattacaaccccggggaggagtatacatgtgggagcaactttgccattgtctatttcatc aacaataacttccagacgtttccccaggcggtgctgctgctcttcaggtgtgcaacaggt gaggeetggeaggagateatgetggeetgteteceagggaagetetgtgaeeetgagtea gtcattggcatgcagatgtttgggaaagttgccatgagagataacaaccagatcaatagg aacaataacttccagacgtttccccaggcggtgctgctgctcttcaggtgtgcaacaggt gaggeetggeaggateatgetggeetgteteceagggaagetetgtgaeeetgagtea Sbjet: 4514 agtttttacatgetetgtgeatttetgateateaatetgttt-gtggetgteategga gtcattggcatgcagatgtttgggaaagttgccatgagagataacaaccagatcaatagg Sbjct: 4454 Sbjct: 4394 Sbjct: 4334 Sbjct: 4274 Query: 409 Query: 469 Query: 349 Query: 229 Query: 289

4592

taatttcgactatctgaccc

Sbjct: 4573

Query: 528

Senal No.: 10/029,413

FIG. 5E

>gb|M83566.1|HUMCACHIA Human neuroendocrine/beta-cell-type calcium channel alpha-1 subunit mRNA, complete cds, Length = 7193

Score = 87.7 bits (44), Expect = 5e-15 Identities = 44/44 (100%)
Strand = Plus / Plus

ctcatcgtaatcggcagcattatagacgtggccctcagcgaagc 4044 ctcatcgtaatcggcagcattatagacgtggccctcagcgaagc Sbjct: 4001 Query: 1

Score = 946 bits (477), Expect = 0.0 Identities = 496/500 (99%), Gaps = 2/500 (0%) Strand = Plus / Plus

4153 aactetgaagagageaatagaatetecateaeetttteegtetttteegagtgatgega 108 Sbjet: 4094 aactetgaagagagaatagaatetecateacetttteegtettteegagtgatgega Query: 49

Sbjet: 4154 ttggtgaagetteteageaggggggaaggeateeggaeattgetgtggaettttattaag 4213 ttggtgaagetteteageaggggaaggeateeggaeattgetgtggaettttattaag 168 Query: 109

228

Query: 169

4572 4453 4513 4393 4333 4273 527 348 288 agtttttacatgctctgtgcatttctgatcatcaatctgttt-gtggctgtcatcatgga aacaataacttccagacgtttccccaggcggtgctgctgctcttcaggtgtgcaacaggt gattacaaccccggggaggagtatacatgtgggagcaactttgccattgtctatttcatc gaggcctggcaggagatcatgctggcctgtctcccagggaagctctgtgaccctgagtca aacaataacttccagacgtttccccaggcggtgctgctgctcttcaggtgtgcaacaggt gtcattggcatgcagatgtttgggaaagttgccatgagagataacaaccagatcaatagg gtcattggcatgcagatgtttgggaaagttgccatgagagataacaaccagatcaatagg teettteaggegeteegtatgtggeeeteeteatageeatgetgttetteatetgeg agnttttacatgctc 4394 Sbjct: 4514 Sbjct: 4454 4334 4214 Sbjct: 4274 469 Query: 409 Query: 349 Query: 289 Query: 229 Query: Sbjct: Sbjct: Sbjct:

4592

taatttcgactatctgaccc

Sbjct: 4573

528

Query: